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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

Claims 6-9, a method for detecting a pathological condition, which is malignancy, comprising detecting the over-or under-expression of the ligand NT-4/5 (SEQ ID NO:45), using as a probe its receptor, SEQ ID NO:2, the truncated form thereof, SEQ ID NO:4, or an immunoadhesin thereof, are examined in the instant application. The embodiment of claims 6-9, as drawn to a method of diagnosis of a pathological condition other than malignancy, using SEQ ID NO:45, or a method for detecting a pathological condition, including malignancy, by detecting the expression of BDNF (SEQ ID NO:42), NT-3 (SEQ ID NO:43) and NT-4 (SEQ ID NO:44), have been withdrawn from consideration as being drawn to non-elected invention. Claims 10-11 have been withdrawn from consideration as being drawn to non-elected invention.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-9 remain rejected under 112, first paragraph, for lack of enablement for a method for diagnosis of malignancy, for reasons already of record in paper of 02/13/08.

1) The nature of the invention

The response asserts that the nature of the claimed invention is routine in the art, since the probes and targets are specifically disclosed, and since the application provides sufficient teaching so that one would know how to practice the claimed methods.

The response has been considered but is not found to be persuasive for the following reasons:

The claimed method is not routine and it would be undue experimentation for one to practice the claimed invention for the following reasons:

1) Although the probe and the target are provided, however, **the claimed receptor probe is not specific** for the target SEQ ID NO:45. One cannot predict whether the non-specific binding of the claimed probe to proteins other than SEQ ID NO:45 would not interfere with or mask the binding data of the claimed probe to SEQ ID NO:45, in view that one cannot predict that proteins other than SEQ ID NO:45 have the same expression level as SEQ ID NO:45 in cancer as compared to normal control. That is, one cannot predict whether said proteins are similarly overexpressed or underexpressed in a particular cancer as SEQ ID NO:45, because expression levels of different proteins in cancers are unpredictable, and are independent of each other, in view of the teaching of Soontornniyooomkij et al and Guate et al, all of record.

2) The claimed method encompasses **detecting a genus of cancers**, using the claimed non-specific probe. Which particular cancer overexpresses SEQ ID NO:45, or which particular cancer other pancreatic cancer underexpresses SEQ ID NO:45 is not predictable, in view that the level of expression of a protein in a particular cancer is not predictable, in view of the teaching of Soontornniyooomkij et al and Guate et al, all of record.

2) The state of the prior art.

The response asserts that Schneider et al demonstrate that one can detect a malignancy, such as pancreatic cancer, by detecting the underexpression of NT-4 (SEQ ID NO:45) using an

antibody to NT-4. The response asserts that both an antibody and a detectably labeled human trkB receptor polypeptide comprising SEQ ID NO:2 or SEQ ID NO:4, or an immunoadhesin thereof capable of binding said neurotrophic factor are effective to bind SEQ ID NO:45. The response asserts that the claimed invention is enabled, regardless whether the art method, using an antibody that would be or would not be more specific. The response recites a case law, which teaches that a claim is not invalid for lack of operability simply because the invention does not work perfectly under all conditions.

The response has been considered but is not found to be persuasive for the following reasons:

Although both the antibody and the claimed receptor probe are capable of binding to SEQ ID NO:45, however, the antibody to SEQ ID NO:45 taught by the art is specific for SEQ ID NO:45, whereas the claimed receptor probe is not specific for SEQ ID NO:45 and would also bind to proteins other than SEQ ID NO:45, the levels of expression of which in cancers are not predictable. Thus one cannot extrapolate the enablement of the art data to the enablement of the claimed method.

Moreover, the case law is not applicable to the instant claimed invention, because under which condition that the claimed method works is not predictable. The instant specification does not have any data nor objective evidence that using the claimed receptor probe, the claimed method would successfully detect a genus of cancers, including pancreatic cancer.

3) The relative skill of those in the art

The response asserts that the claimed methods do not require knowledge of the level of SEQ ID NO:45 that is indicative of cancer, but instead diagnose the selected pathological condition by determining if the level of expression of SEQ ID NO:45 is either a) greater, or b) lesser than the level of expression of SEQ ID NO:45 in a sample from a normal subject. The response asserts that there is no reason to believe that BDNF and NT-3 would be expressed at all, or would be expressed at differential levels in all samples, and so there is no reason to assume that such postulated "interference" would occur or would be a significant factor in the practice of the invention. The response recites a case law, asserting that even if such interference might be possible, a claim is not invalid for lack of operability simply because the invention does not work perfectly under all conditions.

The response has been considered but is not found to be persuasive for the following reasons:

The method requires that the overexpression or underexpression of SEQ ID NO:45 is detected in a genus of cancer, using the claimed non-specific receptor probe. Other than underexpression of SEQ ID NO:45 in pancreatic cancer, whether such overexpression in a cancer, or underexpression of SEQ ID NO:45 in a cancer other than pancreatic cancer exists is not predictable, in view that the level of expression of a protein in a particular cancer is not predictable, in view of the teaching of Soontornniyooomkij et al and Guate et al, all of record.

Moreover, even such overexpression or underexpression of SEQ ID NO:45 in a genus of cancer existed, one cannot predict that such overexpression or underexpression of SEQ ID NO:45 would be detected in cancers using the claimed receptor probe, because the claimed

receptor probe is non-specific. One cannot predict whether the non-specific binding of the claimed probe to proteins other than SEQ ID NO:45 would not interfere with or mask the binding data of the claimed probe to SEQ ID NO:45, in view that one cannot predict that proteins other than SEQ ID NO:45 have the same expression level as SEQ ID NO:45 in cancer as compared to normal control, in view of the teaching of Soontornniyooomkij et al and Guate et al, all of record.

Moreover, the case law is not applicable to the instant claimed invention, because under which condition that the claimed method works is not predictable. The instant specification does not have any data nor objective evidence that using the claimed receptor probe, the claimed method would successfully detect overexpression or underexpression of SEQ ID NO:45 in a genus of cancer, including pancreatic cancer.

4) The unpredictability of the art

The response asserts that the issue of non-specific method, and the detecting a genus of cancer has been addressed above. The response asserts that prior knowledge of absolute levels of SEQ ID NO:45 is not required. The response asserts that the claimed probe binds to the target, so that the claimed method is enabled.

The response has been considered but is not found to be persuasive for the following reasons:

Although prior knowledge of the levels of SEQ ID NO:45 in different cancers is not required, however, one cannot predict that other than underexpression of SEQ ID NO:45 in pancreatic cancer, overerexpression SEQ ID NO:45, or underexpression SEQ ID NO:45 exists in

cancers, in view that the level of expression of a protein in a particular cancer is not predictable, in view of the teaching of Soontornniyooomkij et al and Guate et al, all of record. Further, although the claimed receptor probe binds to SEQ ID NO:45, however, such probe is non-specific. One cannot predict whether the non-specific binding of the claimed probe to proteins other than SEQ ID NO:45 would not interfere with or mask the binding data of the claimed probe to SEQ ID NO:45, in view that one cannot predict that proteins other than SEQ ID NO:45 have the same expression level as SEQ ID NO:45 in cancer as compared to normal control, in view of the teaching of Soontornniyooomkij et al and Guate et al, all of record.

5) The breadth of the claims

The response asserts that the claims are not broad, because the methods are limited to specific steps that require the use of identified molecules. The response asserts that the claimed methods require the use of detectably labeled SEQ ID NO:2 or detectably labeled SEQ ID NO:4, or an immunoadhesin thereof; and require detecting binding of these molecules to SEQ ID NO:45.

The response has been considered but is not found to be persuasive for the following reasons:

The claims are broad, encompassing a method for diagnosis of numerous cancers, which either overexpress or underexpress SEQ ID NO:45, using a receptor probe which is non-specific for the target SEQ ID NO:45.

6) The amount of direction and the absence of working example.

The response asserts that the specification and the art provide evidence that one of ordinary skill in the art could use to enable the practice of the invention by using detectably labeled SEQ ID NO:2, SEQ ID NO:4. or an immunoadhesin thereofi to detect SEQ ID NO:45 in test samples and in samples from normal tissue, thereby to diagnose a malignancy characterized by overexpression or underexpression of SEQ 1D NO:45. The response asserts that the specification and the art provide evidence that SEQ ID NO:2, SEQ 1D NO:4. or an immunoadhesin thereof', bind SEQ ID NO:45, and thus that these molecules are suitable and effective probes, and suitable for the practice of the claimed invention.

The response has been considered but is not found to be persuasive for the following reasons:

Although the specification and the art disclose how to measure the level of the neurotrophic factor, however, the specification and the art do not disclose, nor have any concrete evidence of which cancer over-expresses the claimed neurotrophic factor, SEQ ID NO: 45, or which cancer other than pancreatic cancer underexpresses SEQ ID NO:45, as compared to the normal corresponding control, such that SEQ ID NO:45 could be used for diagnosis of the claimed genus of cancers. Further, the specification nor the art do not have any data, or concrete evidence that the trkB receptor, SEQ ID NO: 2, SEQ ID NO:4 or an immunoadhesin thereof is a suitable, specific probe, and only detects the ligand NT-4/5 (SEQ ID NO:45), such that the claimed receptor probe could be successfully used for detecting cancers.

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the

claimed invention, it would have been undue experimentation for one of skill in the art to practice the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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MINH TAM DAVIS
May 12, 2008

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643